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Somatosensory Symptoms and Signs and Conditioned Pain Modulation in Chronic Post-Stroke Shoulder Pain

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Abstract: Persistent shoulder pain is a common complication after stroke. Its etiology and underlying mechanisms are not well understood and treatment is generally unsatisfactory. The objective of this study was to assess the role of central sensitization and disinhibition in chronic stroke patients with chronic PSSP (n = 19), pain-free stroke patients (n = 29), and healthy controls (n = 23). Positive and negative somatosensory symptoms and signs were assessed using clinical examination and electrical and mechanical quantitative sensory testing (QST). Conditioned pain modulation (CPM) was assessed by comparing QST thresholds before and after applying a cold pressor test. Sensory abnormalities were more frequently observed and more severe in patients with PSSP, including positive signs such as allodynia at the affected side and generalized hyperalgesia at the unaffected side. CPM was similar in stroke patients and healthy controls. This study showed that chronic PSSP was associated with several positive and negative somatosensory signs, implicating a role for central sensitization and possibly for disinhibition. Since the causal relationship remains unclear, and may be related to either neuroplasticity induced by ongoing nociception as well as to the neuropathic brain lesion, prospective studies are warranted.

***Perspective:** The assessment of somatosensory symptoms and signs and endogenous pain modulation demonstrated a role for central sensitization and possibly for disinhibition in chronic PSSP. Prevention and treatment of PSSP could benefit from a more detailed analysis of both peripheral and central pain mechanisms.*

***Key words:** Stroke, shoulder pain, somatosensory function, quantitative sensory testing, conditioned pain modulation, diffuse noxious inhibitory controls.*

Pain is a common complication after stroke.[20,33] Post-stroke pain is a great burden for the patient and impedes rehabilitation.[46,56] One of the most reported types is post-stroke shoulder pain (PSSP) which typically develops at the affected side after 2 to 3 months.[13,15,20,41] Although its etiology is largely unknown, several clinical conditions such as spasticity, glenohumeral subluxation, capsular inflammation, peripheral neuropathy, central post-stroke pain (CPSP), and autonomic dysfunction have been related to PSSP.[48,51,63] Furthermore, several studies have suggested that reduced motor function,[14,15,17,31,33,39] depression,[14,15,33] and reduced somatosensory function[14,15,17,33,35,60] may contribute to the development of PSSP. Clinical presentations of PSSP, CPSP, and post-stroke complex regional pain syndrome

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type 1 (shoulder-hand syndrome) may show considerable overlap complicating the diagnosis and prognosis of post-stroke pain.[24,45]

PSSP may resolve spontaneously in the course of rehabilitation, but is persistent (>12 months) in 65% of the patients.[31] The evidence for effective therapeutic interventions for PSSP is lacking or inconsistent and, in the case of successful treatment, it is often unclear what mechanisms have been responsible for the pain reduction.[42] Together, this suggests that the pain mechanisms underlying PSSP development and maintenance may be more complex than previously realized, and that the traditional view and approach of PSSP as purely ongoing nociceptive pain may need revision.[45]

The assessment of positive and negative somatosensory symptoms and signs in relation to the pain complaints is 1 of the first steps towards a better understanding of pain mechanisms.[43,44] Although the relationship between symptoms and signs and pain mechanisms is still under debate,[18] several symptoms and signs, such as sensory loss (eg spinothalamocortical tract lesions), allodynia, and generalized hyperalgesia, have been associated with experimentally induced central sensitization[21,25,58] and/or various forms of chronic nociceptive[47] or neuropathic[6,10,57] pain. In addition, endogenous pain modulation, involving supraspinal diffuse noxious inhibitory controls (DNIC),[29] has been shown to be impaired in various types of chronic pain, such as painful osteoarthritis,[28] whiplash,[22] and neuropathic pain.[61] So far, little is known about the role of central sensitization or disinhibition in the development and maintenance of PSSP.

The objective of this study was to assess the role of central sensitization and disinhibition in chronic stroke patients (>6 months post-stroke) with chronic (duration >3 months) PSSP (n = 19), pain-free stroke patients (n = 29), and healthy controls (n = 23). Positive and negative somatosensory symptoms and signs were assessed using clinical examination and electrical and mechanical quantitative sensory testing (QST). Conditioned pain modulation (CPM) was assessed by comparing QST thresholds before and after applying a cold pressor test. It was expected that both the frequency as well as the severity of somatosensory abnormalities would be higher in the patients with PSSP and that, in addition to previously reported associations with negative signs, PSSP would be associated with positive somatosensory symptoms and signs indicative of central sensitization and/or disinhibition such as allodynia, generalized hyperalgesia, and impaired endogenous inhibitory pain modulation.

Methods

Subjects

This study included stroke patients with persistent shoulder pain (PSSP, n = 19), pain-free stroke patients (PF, n = 29), and healthy controls (HC, n = 23). Stroke patients were recruited in 2 regional rehabilitation centers in the Netherlands (Roessingh Rehabilitation Center in Enschede and Sint Maartenskliniek in Nijmegen). The outpatient databases were searched for stroke patients who had been hospitalized in the 2 years prior to the start of inclusion (Fall 2007). Patients fulfilling the inclusion and exclusion criteria were approached by mail. In addition, patients visiting the outpatient clinics with shoulder pain complaints were asked by their treating physician if they could be approached by 1 of the researchers (M.R.) by mail. Healthy subjects (age 40–60) were recruited through advertisements in local community centers and newspapers.

All stroke patients were 18 years or older and sustained a unilateral brain infarction with an onset at least 6 months prior to participation. For stroke patients to be included in the PSSP group, shoulder pain had to be unilateral, be confined to the affected side, have an onset after stroke, and be persistent (daily pain, duration longer than 3 subsequent months). Patients were included in the PF group if they had no long-lasting (>1 week in the last 3 months) pain complaints. Exclusion criteria were: Pregnancy, trauma, infection, signs of any possible concomitant neurological condition (eg, multiple sclerosis, HIV/AIDS, peripheral neuropathy), not being able to reliably determine sensory thresholds during a training session prior to the experiment, and other pain complaints than simple shoulder pain (eg, CPSP,[24] wide-spread pain, or shoulder-hand syndrome). Healthy control subjects had to be free of any neurological or psychiatric disorder, diabetes mellitus, psychotropic medication, or long-lasting (>1 week in the last 3 months) pain complaints. When subjects considered for the PF or HC groups reported minor pain complaints at the time of the experiment, the experiment was postponed until subjects were pain-free for at least 2 weeks. The study was approved by the human ethics committee of the Roessingh Rehabilitation Center in Enschede, the Netherlands. All subjects received written and oral information about the study protocol and all participants gave informed written consent prior to their participation.

Demographic Data and Medical Examination

General demographic characteristics such age, gender and (for the patients) lesion side, stroke onset, and medication use were registered. Shoulder pain was evaluated both at rest and during movement with an 11-point Numeric Rating Scale (NRS, 0 = no pain, 10 = maximum conceivable pain). The emotional state was assessed using the ZUNG self-rating depression scale (score: 20–80) which has been validated for both healthy subjects and stroke patients.[50] Cognitive state was assessed using the Mini Mental State Exam (MMSE, score: 0–30, cognitive impairment was defined as a MMSE score <24).[49] Physical examination included the assessment of trophic changes in the arms and hands (severe color or perspiration changes or asymmetry, edema, assessed by visual inspection and subject reports), glenohumeral subluxation (assessed by palpation, scored in steps of 5 mm), pain-free range of motion for passive shoulder elevation (0–180 degrees) and external rotation (0–90 degrees),